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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/988,971	11/20/2001	Han Chang	D0043 NP	9658

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/988,971	**Applicant(s)** CHANG ET AL.	
	Examiner Michail A. Belyavskyi	**Art Unit** 1644	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 27 June 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *27 June 2005*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: ----.

   Claim(s) objected to: ----.

   Claim(s) rejected: *21-25,31,33-35 and 41-45*.

   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see continuation sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

S.V.O

1. Claims 21-25, 31, 33-35 and 41-45 are rejected under 35 U.S.C. 101 as the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the same reasons set forth in the previous Office Action, mailed 12/27/04.

Applicant's arguments, filed 06/27/05 have been fully considered, but have not been found convincing.

Applicant assets that : (i) one skilled in the art would reasonable believed that hSLAP-2 is a new member of the SLAP family of adapter proteins based upon the evidence provided in the instant specification , (ii) as stated in paragraph 76 of the instant specification that hSLAP-2 is a "negative regulator of intracellular signal transduction in several cell types including T cells; (iii) as disclosed by Pawson et al and Pandey et al, the presence of SH2/SH3 domain alone is sufficient evidence to demonstrate that hSLAP-2 is an adaptor protein ;(iv) claimed hSLAP-2 polynucleotide has a substantial utility that is exemplified by the fact that unregulated cellular proliferation and uncontrolled clonal expansion in B-cells can result in B-cell tumors, lymphomas and leukemias; (v) claimed hSLAP-2 polynucleotide have a well established utility due to its significant homology to known adaptor proteins, particularly SLAP family member and shared expression profile to other SLAP family member and pointed to the teaching of Holland et al., Pandey et al and Loreto et al. Each of these assertions will be addressed individually.

First, as was stated in the previous Office Action, the specification disclosed a novel nucleic acid molecules of SEQ ID NO: 1 encoding SH2/SH3 domain –containing protein h SLAP-2 of SEQ ID NO:2. The specification fails to provide sufficient objective evidence of any activity for encoded protein. Applicant only states that said protein shows 47 % identity to human SLAP and 58 % identity to the mouse SLAP proteins (see Table 4 and page 61, lines 22-30 in particular). The specification disclosed that based on sequence homology to related molecules , said protein may be a novel human SLAP-2 protein. The specification also disclosed that said hSLAP-2 nucleic acid sequence and related protein can be used for diagnosing, treating or preventing disorders or diseases associated with aberrant or uncontrolled cellular signal transduction or with hyperactive cell, or may play a role in one or more aspects of regulating the immune system and tumor cell biology (see page 20, lines 5-20 and page 41, lines 22-30 in particular). No well-established utility for a human SLAP-2 protein is indicated. Moreover, in addition to previously cited references indicating that homology –based prediction of protein function is unreliable, newly cited references of Whisstock et al., (Quarterly Review of Biophysics, 2003, 36, pp307-340) teaches that prediction of protein function from sequence and structure is difficult problem, because homologous proteins often have different function. A fundamental problem is that function is in many cases an ill-defined concept (see Abstract in particular). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Thus, in light of the art recognized fact that minor sequence differences can significantly affect a protein's function, one skilled in the art would find it more likely than not that h SLAP-2 of SEQ ID NO:2 is not having the same function as human SLAP. The recitation of percent identity language, in the absence of a testable function and limitations regarding the sequence length over which the percent identity is required does not allow the skilled artisan reasonable believed that hSLAP-2 is a new member of the SLAP family of adapter proteins. Thus, the homology-based assignment h SLAP-2 of SEQ ID NO:2 as human SLAP receptor does not appear to provide evidence of a specific and substantial utility based on the knowledge of the skilled artisan and the data presented in the instant specification.

Second, in paragraph 76 of the instant specification it is clearly stated that SLAP, not hSLAP-2, have been shown to be a negative regulator of intracellular signal transduction in several cell types including T cells.

With regard to the teaching of Pawson et al., and Pandey et al, the Examiner disagree with the Applicants interpretation of said references. Pawson et al., merely teach role of scaffold, ancoring and adaptor proteins that contribute to the specificity of signal transduction events by recruiting active enzymes into signaling network (see entire document, Abstract in particular). Moreover, Pawson et al., teach that different types of proteins may have several interacting domains including PDZ, SH3 and LIM domains and that covalent associating of these recognition modules as found in adaptor ancoring and docking proteins allows a single peptide to bind multiple protein ligands. As an added complexity a single module can bind either to a motif within the same molecule or in an intermolecular fashion to other proteins (see page 2079 in particular). Similary, Pandey et al. teach that adapter proteins contain a variety of modular domains that mediate protein-protein interaction and further that a number of adapter proteins have been isolated , some of them have positive regulation while others have negative regulation (see entire document, page 19131 in particular. No single effect of the disclosed hSLAP-2 is ascribed to the claimed protein and the original members of the family were not classified based on their biological activity, but rather, by their common structure and the fact that they are adaptor proteins. Without some common biological activity for the family members, a new member would not have a specific, substantial, or credible utility when relying only on the fact that it has structural similarity to the other family members and is also a adaptor protein. The members of the family have different biological activities which are related to regulation of intracellular signal transduction in several cell types including T cells, but there is no evidence that the claimed compounds share any one of those activities. The rejection was based on the failure to disclose sufficient properties of SH2/SH3 domain –containing protein h SLAP-2 of SEQ ID NO:2 to support an inference of utility. The adaptor subfamily to which the polypeptide belongs is a family in which the members have divergent functions. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. To argue that all the members can be used for "regulation" of intracellular signal transduction in several cell types including T cells is to argue a general, nonspecific utility that would apply to virtually every member of the family, absent evidence to the contrary. Further, any compound could be considered as regulator or modulator of a tissue in that any compound, if administered in the proper amount, will stimulate or inhibit a tissue. For example, salt, ethanol, and water are all compounds which will kill cells if administered in a great enough amount, and which would stimulate cells from which these compounds had been withheld, therefore, they could be considered regulators or modulators of epithelial tissue. However, use of these compounds for the modulation of epithelial tissue would not be considered a specific and substantial utility unless there was some disclosure of, for example, a specific and particular combination of compound/composition and application of such in some particular environment of use.

With regards to the fact that unregulated cellular proliferation and uncontrolled clonal expansion in B-cells can result in B-cell tumors, lymphomas and leukemias. This arguments is not disputed, however, the issue raised by the Examiner in the previous Office Action was that

the specification does not disclose any diseases or conditions known to be associated with the hSLAP polypeptide , encoded by SEQ ID NO:2 or any conditions associated with altered levels (increase or decrease) of said polypeptide. Since any protein may potentially be used as a treatment agent, this utility would not be considered to be specific. Since no particular disease or condition is disclosed, the artisan would have been required to perform additional experimentation to identify and/or reasonably confirm the asserted use of hSLAP polypeptide as a treatment agent and therefore, this utility would not be considered to be substantial.

With regards to the teaching of Holland et al., Pandey et al and Loreto et al. , that hSLAP-2 polynucleotide have a well established utility due to its significant homology to known adaptor proteins, particularly SLAP family member . Although said papers teach that hSLAP-2 protein may have similarities to SLAP nowhere in said papers there are indications or teaching that hSLAP-2 indeed have the same function as SLAP protein. Moreover, Holland et al., teach that although SLAP-2 and SLAP share structural homologies their mechanisms of action is different and further studies are required to determine the role and function of SLAP-2 protein (see overlapping pages 1273 –1274 in particular). Similarly, Pandey et al. teach that C terminus of SLAP-2 is not very similar to that of SLAP ant it lacks the last 27 amino acid found in SLAP (see page 19137 in particular). Thus, after further research, specific and substantial utility might be found for claimed polypeptide h SLAP-2 of SEQ ID NO:2. This further characterization, however is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. A well-established utility is a specific, substantial, and utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material.

As such, further research would be required. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966), the court indicates "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." A patent is therefore not a license to experiment. Because the claimed invention is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

2. Claims 21-25, 31, 33-35 and 41-45 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial, asserted utility or a well established utility for the reasons set forth in the rejection under 35 USC101 above, one skilled in the art clearly would not know how to use the claimed invention for the same reasons set forth in the previous Office Action, mailed 12/27/04.

Applicant's arguments, filed 06/27/05 have been fully considered, but have not been found convincing.

Applicant argue that since hSLAP-2 has a specific, substantial and well established utility, one skilled in the art clearly would know how to use the claimed invention.

Contrary to Applicant's arguments as was stated above under 35 USC101 , it is the Examiner position that the claimed invention is not supported by either a specific and substantial, asserted utility or a well established utility thus one skilled in the art clearly would not know how to use the claimed invention.

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